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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,821	02/27/2004	Revital Lifshitz-Liron	1662/62902	8234
26646 7590 06/21/2007 KENYON & KENYON LLP ONE BROADWAY NEW YORK, NY 10004			EXAMINER DESAI, RITA J	
			ART UNIT 1625	PAPER NUMBER
			MAIL DATE 06/21/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/789,821	Applicant(s) LIFSHITZ-LIRON ET AL.	
	Examiner Rita J. Desai	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 April 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>4/9/07</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/9/2007 has been entered.

The previous rejection of claims 1-12 under 35 USC 103 (a) over U.S. Patent Application Publication No. 2004/0181086, attributed to Javdani, Cattaneo, AN EXPERIMENT WITH ACID MINE WATER, U.S. Patent No. 4,594,466 to Reeves, Kegley, WATER TREATMENT, Hayes, 6.2.2.1, SELECTIVE PRECIPITATION, IUPAC Compendium of Chemical Terminology, (IUPAC), chm.vt.edu (VT), Angel C. de Dios, Le Chateliers Principle, Lecture VIII, Chem 056 (de Dios), Complexation and Precipitation Titrations (Complexation), Volumetric (Titrametric) Analysis (Volumetric Analysis), Protein Purification Handbook (the Handbook), and Solubility of Ionic Salts in Water: Precipitation Titrations (Ionic Salts) still stands.

Applicants argue that

" the presently claimed invention is directed to a process for purifying zoledronic acid. The presently claimed process comprises: (a) raising the pH of an aqueous suspension of crude zoledronic acid until a clear solution is obtained; (b) lowering the pH of the solution obtained in (a) until purified zoledronic acid precipitates out of solution; and (c) isolating the purified zoledronic acid that has precipitated from the solution in (b). That is, in the presently claimed process, the pH of a suspension of crude zoledronic acid is raised until a clear solution is obtained; the pH of the clear solution is then lowered until purified zoledronic acid precipitates out of solution; and the precipitated purified zoledronic acid is then isolated. "

A clear solution will be obtained if the impurities are such, that they would dissolve in the base.

The pH is lowered to obtain the precipitated Zoledronic acid, the pH of which will depend on the pKas of the acid.

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Separating and isolation of compounds by changing the pH is routine experimentation for a chemist. For example lab manuals for Chemistry courses routinely teach isolating techniques. e.g. University of Alberta lab manual shows the isolation of bromobenzoic acid.

Separation of acids, bases and neutral compounds

INTRODUCTION

As a chemist, you will be dealing with complex mixtures of many compounds.

Almost always when you carry out a preparative experiment, you will need to separate the product from the reaction mixture.

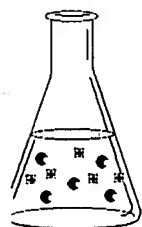
At other times, you will want to isolate a specific natural product from plant or animal tissue.

Therefore, the separation and purification of compounds are very important task(s) for an organic chemist.

Acid-base extraction, the technique you will learn in this site (and in the lab) is a powerful method to separate organic compounds of different solubility classes:

organic acids, organic bases, and neutral compounds.

Dividing the components of a mixture by solubility is usually done at the beginning of the isolation of a complicated natural product mixture.



Isolation of 2-bromobenzoic acid

OK, Let's isolate 2-bromobenzoic acid from the solution which contains it.

- The basic aqueous solution contains the salt of 2-bromobenzoic acid, sodium 2-bromobenzoate.
- You want to change sodium benzoate (salt of an organic acid) to the water-insoluble benzoic acid (organic acid) by converting the salt to a protonated, non-ionic form.

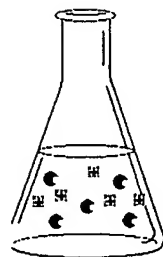
Symbols

- 2-bromobenzoate anion
- Sodium cation
- 2-bromobenzoic acid
- Proton (H^+)
- Hydroxide ion

Which solution will you add?

- ☐ dilute aqueous HCl
- ☐ dilute aqueous NaOH
- ☐ conc. HCl
- ☐ conc. NaOH

ADD Clear



- You need to add concentrated HCl until the solution becomes acidic. This process is called acidification.

- In an acidic solution, 2-bromobenzoic acid is completely protonated and no longer very soluble in aqueous solution.

Symbols

- 2-bromobenzoate anion
- Sodium cation
- Chloride ion
- Proton (H^+)
- 2-bromobenzoic acid

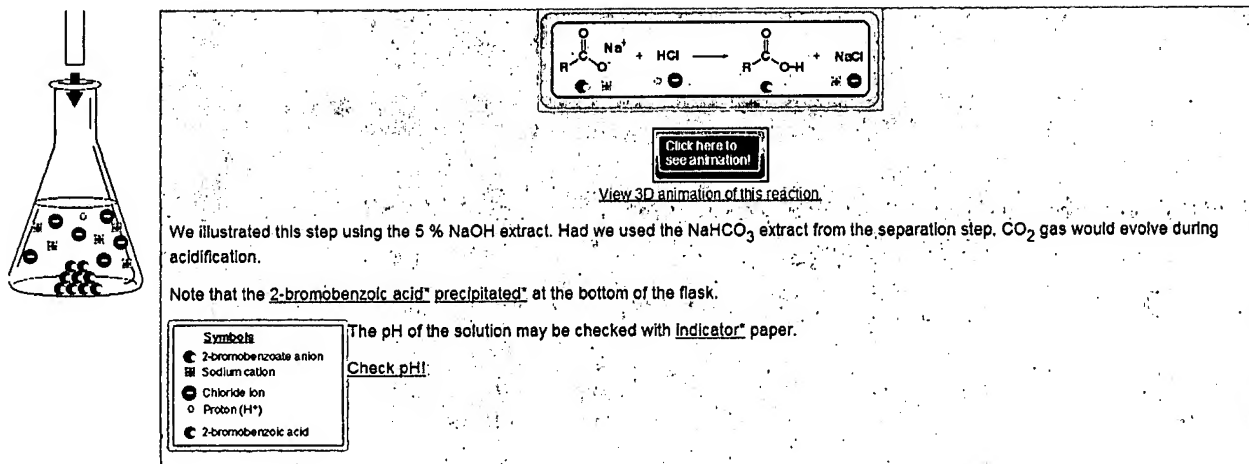
OK, click ADD to add conc. HCl dropwise until the solution becomes acidic.

Watch what happens after each addition!

ADD

Organic Web Chem University of Alberta

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When NaOH is added the sodium salt in solution (clear solution) is formed and then when the acid is formed, depending on the pKa of the acid it will precipitate out.

Applicants claims do not indicate the crudeness of the starting Zoledronic acid.

The impurities and the extent of purification.

Nor does the claim specifically indicate the "improvement" in the purification process.

Limitations of the specifications (as to which impurities are removed and the final purity) cannot be read into the claims.

In general purification of compounds is a routine experimentation for a chemist in that field and one of skill in the art would be motivated to remove impurities by changing pH or solvent, or standard conditions.

Applicants are correct the Publication 20040171872 is the corresponding publication of application number 10/472962 which is what the examiner had meant to use.

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Applicants further argue that all the references cited would teach that once the pH was raised all the acids would dissolve to form a clear solution and then as the pH was lowered all the components would precipitate out leaving the mixture the same as what they started with.

This is not found to be convincing, as the claim does not recite the impurities nor the amount of impurities present at the start.

The support that applicants have in the specifications is of the impurities imidazoyl and IAA which is so small that it does not make a purer form of a known compound more patentable. As purification/isolation/ separation techniques are routine experimentations to a chemist.

In re Aller et al 105 USPQ 233. *The selection of reaction conditions is mere optimization by mere modification of routine experimentation and within one skilled in the art . Change in temperature , concentration , or both is not patentable modification in the absence of unexpected results which is different in kind and not in degree.*

Conclusion

Claims 1-12 still stand rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas McKenzie can be reached on 571-272-0670. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Rita J. Desai
Primary Examiner
Art Unit 1625

R. Desai
6/18/07

R.D.
June 18, 2007